

Applicants: Jane H. Morse and James A. Knowles  
Serial No.: 09/904,380  
Filed : July 12, 2001  
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**REMARKS**

Claims 1-5, 7, 8, 10-19, 21-49, 51, 52, and 56 are pending in the subject application. By this Amendment, applicant has canceled claims 7 AND 8 without prejudice. Claims 1-4, 10, 12, 14, 16, 18, 21, 23-31, 33-35, 37, 39-48, 51, 52 have been amended to make certain formatting changes. Accordingly, claims 1-5, 10-19, 21-49, 51, 52, and 56 will be pending and under examination in the subject application upon entry of this Amendment.

In view of the arguments below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

**Rejection under 35 U.S.C. §112, First Paragraph**

The Examiner rejects claim 1-5, 7, 8, 49, 51 and 52 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that the specification only provides a written description of the specific mutations as set forth in Figure 4 of the subject application.

In response, applicants respectfully traverse the Examiner's rejection.

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The test for written description under 35 U.S.C. §112, first paragraph, is whether the disclosure describes the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. According to M.P.E.P. §2163(I)(A), when evaluating whether support in the specification for the original claims is sufficient, "[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). The initial burden is therefore on the Examiner to present evidence of the lack of written description. Applicant maintains that the claimed invention satisfies the test for adequate written description, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

The subject invention provides methods of detecting whether a subject is either predisposed to or afflicted with pulmonary hypertension by detecting whether a mutation is present within the bone morphogenetic protein receptor-II (BPMR-II) gene. This invention is based on applicants' discovery of the role of mutations of the BPMR-II gene in pulmonary hypertension.

In support of the rejection, the Examiner alleges that a representative number of species have not been described by complete structure or by sufficient relevant identifying characteristics. The Examiner further alleges that there is no description of mutations which occur in the BPMR-II gene.

Applicant disagrees with the Examiner's position. As the Examiner concedes the specification discloses 19 gene-level

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mutations and their corresponding amino acid-level mutation. These mutations are identified in the instant specification, *inter alia*, at page 16, line 5 to page 23, line 17, summarized in Figure 4, by their location on the BMPR-II gene, i.e. exon number, their DNA sequence variation, i.e. deletion, insertion, or substitution of nucleic acids, and their corresponding protein sequence variation. In addition, Figure 2 schematically details the intron/exon structure of the BMPR-II gene and the corresponding mutations, both mutations that cause premature termination of BMPR-II and those found in Arg491.

Moreover, according to M.P.E.P. §2163 (II)(A)(3)(a)(ii), the written description for a claimed genus may be satisfied by disclosure of relevant, identifying characteristics sufficient to show the applicant was in possession of the claimed genus. *Regents of the University of California v Eli Lilly*, 119 F3d. 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). Satisfactory disclosure depends on whether the necessary common attributes of the genus are recognized by one skilled in the art in view of the species disclosed. It does not require that the description be so specific as to fully describe all species in the genus. Applicants maintain that the claimed genus is supported by the disclosed species, and that the species disclose the necessary attributes of the claimed genus.

The claimed genus comprises mutations located on the BMPR-II gene which have been associated with the predisposition and onset of pulmonary hypertension. The disclosed species include 19 such mutations. Claim 1 provides a method of

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detecting a subject's predisposition to or affliction with pulmonary hypertension by detecting whether a mutation is present within the bone morphogenetic protein receptor-II (BPMR-II) gene. In assessing three potential gene candidates, CD28, CTLA4 and BPMR-II, applicants identified BPMR-II as the gene with mutations common to those afflicted with pulmonary hypertension. The location of these mutations on the BPMR-II gene is one of the common attributes of the claimed genus. One skilled in the pertinent art would recognize this attribute as a potential diagnostic tool. Accordingly, applicants maintain that one skilled in the art would easily recognize the commonality of the claimed genus in view of the disclosed species.

In view of these remarks, applicants maintain that claims 1-5, 49, 51 and 52 are adequately supported by the disclosure and satisfy the requirements of 35 U.S.C. §112, first paragraph.


#### **Summary**

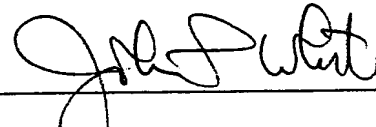
In view of the arguments set forth above, applicants maintain that the Examiner's rejections have been overcome. Applicants respectfully request that the Examiner reconsider and withdraw same, and earnestly solicits allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee, other than the enclosed \$205.00 for the two-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450	
	9/26/03
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